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Book title: Infectious and Invasive Diseases of Horses, Selkhozgiz, Moscow, 1954; 558 p.

V. M. Lekareva

Extract: Infectious Encephalomyelitis. p. 269-290.

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Infectious encephalomyelitis (IEM) of horses is an acute infectious disease. It is caused by a neurotropic filterable virus and is accompanied by a disruption of the activity of the nervous system, jaundice of the mucous membranes and with a distinctly expressed paresis of the gastro-intestinal tract. This illness is observed as an enzootic of sporadic cases and very seldom as an epizootic.

HISTORICAL references: A disease of horses with signs of affection of the central nervous system has been known for a long time. Separate data on this illness are encountered in literature of the 18th century. P. M. Makarov published data on the significant distribution of this infection in the period 1900-1912 in various provinces of Russia. According to the material of the horse-breeders of the Northern Kavkaz, it was noted in 1902 and then repeated itself after 3-5 years until 1939.

In regard to the etiology of this illness there were many various suppositions made. Bannikov, Naimov and Sidorov regarded it as a fodder poisoning.

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The greatest attention to the study of IEM was appropriated in the period 1925-1936. Expeditions consisting of epizootologists, bacteriologists, pathologo-anatomists, clinicians and other specialists expressed different points of view on the etiology of this disease on the basis of the data obtained. Thus, one of the expeditions, in the organization of which were included the presidents of Scientific-Research Institutes of the Ukraine, reported that Spirochaeta, which according to the supposition of the commission was the agent of the illness, was found in the

Submitted by V. M. Lekareva

spinal fluid of horses which had been ill and died from a meningo-like disease(ILE). This supposition of the Ukraine expedition was not confirmed during a later more accurate study. S. N. Veshelesski and other authors proved that this Spirochaeta was easily detected in the spinal fluid of healthy horses as well, and in other animals, and therefore cannot play any etiological of specific role.

The un-based opinions of various authors on the cause of the disease were quickly rejected, which stipulated the appearance of new points of view, and consequently, new trends in the study of the etiology of IEM.

A Russian scientist, D. I. Ivanovski, correctly approached the study of filterable viruses 60 years ago. His discovery of the filterable virus of the mosaic disease of tobacco served as the start of the study of the nature of filterable viruses. He developed the method which has been accepted for the study of filterable viruses which cause diseases in man and animals.

S. N. Veshelesski, using the method of studying filterable viruses and infecting cats with pathological material from dead horse, isolated a filterable virus and proved its etiological importance. I. G. Levenberg, using this same method, obtained positive results during infecting of rabbits. These two tests served as evidence of the virus nature of diseases.

A proper name was obtained with the establishment of the etiology of the disease--infectious encephalomyelitis of horses(IEM).

Diseases of horses with an affection of the central nervous system are encountered in almost all countries.

We will set here a short description of encephalides of an infectious nature which are observed in various countries.

THE BORNA disease was first described in 1878 in Saxony(central Germany), in the Borna region, from where it got its name.

The agent of the encephalomyelitis of horses in Germany was studied by Tsvik and regarded as a filterable virus. The illness progresses in an acute or sub-acute form and is terminated most often with the death of the animal. Of laboratory animals, rabbits are susceptible to the virus. The latter always become ill during injection of pathological material into them intracerebrally or subdurally. Guinea pigs, rats and monkeys are also sensitive to the virus. The incubation period lasts from 28 to 40 days, and more, the illness last 10-14 days ordinarily. Horses contract the disease in the rural areas only.

A periodicity of outbreaks is noted, they repeat themselves after several years. The Borna disease is registered in the spring-summer period. The sources and paths of infection are not definite. They consider that the virus can be isolated from the saliva, nasal mucus and urine. The paths of infection, as some authors suppose, can be the mucous membranes of the nose and mouth cavity; the possibility of the penetration of the virus through the digestive tract is not excluded. The possibility of infecting animals by means of direct contact has been proven. On the basis of the length (to ten years) stability of the virus in a dry state, many authors consider the disease to be a ground infection.

In the horses, at the start of the infection, there are observed nervous appearances which develop slowly, by their character completely different and un-constant. The disease is often accompanied by paralysis of the lips, eyelids, tongue and gullet. Defecation is noted, constipation interchanges with diarrhea. A light colic is also noted.

The death-rate of horses during the Borna disease is very high (from 5 to 90%). During dissection no pathologic-anatomic variations are noted. Histologic studies always disclose very characteristic changes in the

Ammon horn and in the other sections of the brain; perivascular infiltration, consisting of plasmatic and lymphoid cells, proliferation of the ganglios cells. In the nuclei of the ganglios cells there are noted intranuclear acidophilic incorporations, without structure, usually surrounded by light thin rims (Joest bodies). The incorporations are easily differentiated from the Negri corpuscles (bodies), which are distributed not in the nuclei, but in the cytoplasm and possess a basophilic structure.

According to certain clinical signs the Borna disease is reminiscent of the rarely encountered in our country IEM of horses. The distinctive signs of the Borna disease are the duration of the disease (from 3 to 24 days, seldom to 6 weeks), weak icterus of the mucous membranes. In the surviving horses there is often observed an after-effect, affection of the nervous system (epileptic fits, paralis, denervation of certain muscles, distortion of vision, etc.).

ENZOOTIC encephalomyelitis of horses in France is observed mainly as sporadic cases. It is insufficiently studied.

Mussin and Marshan described an enzootic outbreak. They observed 15 sick animals, of which 6 fell. According to these authors, the illness has a severe course, lasts from 20 hours to 6 days. Rabbits, which are infected intracerebrally and intramuscularly with a brain suspension from a dead horse, are susceptible to the virus. The incubation period during infection with a virus fixed for rabbits is 3-4 days. During dissection there is always noted an enlargement of the spleen, general septicemia with parenchymatous variations in the liver and kidneys. In the brain during histological studies, besides the variations which indicate encephalomyelitis, there are observed hemorrhages. Incorporations of Joest bodies are not disclosed.

Infections of horses with IEM have been established in Japan also.

According to the data of Emota and Kando, it is caused by two types of virus: one similar to the Borna virus, and the other with the American western variant of encephalitis virus.

There are data which indicate distribution of the IEM of horses in Finland, Rumania and Czechoslovakia.

AMERICAN ENCEPHALITIS. In 1931 meyer, Gering and Govit, during study of an acute form of encephalitis which is encountered in the USA, isolated a filterable virus from the brain tissue of an ailing horse and determined it to be the agent of the disease. Later works established that there are two variants of virus in America--eastern and western.

In 1936 Bik and Vukov showed that a virus isolated in Venezuela differs from the eastern and western variants of virus. The western and eastern viruses differ from each other by virulence, dissemination and immunobiological properties. In certain years this disease takes on a wide measure. In the years 1935-1937 there were 276,000 cases of the disease registered, the mortality consisted of 25-50%. The eastern virus causes a great death rate. A strict seasonality is noted as a characteristic of the disease (June-September in the western states, August-October in the east). There is a noted recurrence which repeats itself after various periods of time. The scattered nature of the centers, the simultaneous infection of animals in sections far removed from each other, do not allow for any conclusion on the exact dissemination of the infection.

Kelser proved(1933) that the disease can be transferred from a sick animal to a healthy one by the mosquito *Aedes aegypti*. Mosquitoes, 6-8 days after sucking blood from infected guinea pigs, infected healthy guinea pigs by biting, horses as well. Later tests established that the virus of IEM is carried by the mosquitoes of other types: *Aedes albopictus*, *A. nigromaculatus*, *A. dorsalis*.

The establishment of the fact that the IFM of horses is vectored by mosquitoes and ticks, and also the finding of the virus in spontaneously infected pheasants and sparrows, allow us to speak of an expansive circulation of the virus in nature among the birds, animals and blood-sucking arthropodes and of the carrying of the infection from the ailing animals to the healthy by the latter.

Many cases of transmission of the virus by contact by means of the mucous membranes of the nose and mouth surfaces are described.

The experimental infection of horses is always successful by the intracerebral method. The horses become infected less often during introduction of the virus subcutaneously, intermuscularly or intercutaneously. Guinea pigs are susceptible to both variants, to a lesser degree—white mice, rabbits and monkeys, and besides these, pheasants, chickens and ducks. Dogs, swine and cats are also susceptible to the eastern virus.

The incubation period in horses in natural conditions lasts to 3 weeks, during experimental infection—3-8 days.

THE CLINICAL chart of the disease in horses is very different. Prodromal appearances are accompanied by disruptions of digestion and insignificant increases in temperature to 39.5 C. An acute onset often starts with a sudden sharp excitation, appearances of convulsions, grinding of the teeth, abrupt movements, inclinations to go forward; during this the horse often suffers bruises, wounds, in a laying position it beats its legs. Then a full loss of sensitivity begins, paralysis of the lips, ears, the action of the gullet is disrupted, the tongue drops out, paresis of the extremities. In the termination of the disease the temperature is ^{sub}normal. The length of the disease is 3-8 days, less often to 24 days.

THE PATHOLOGANATOMICAL chart is characterized by icterus of the mucous membranes, enlargement and sappiness of the lymphatic nodes, a weakly expressed degenerative variation in the liver and kidneys. The brain is

edematous, its vessels injected. The spleen is without visible changes. Histological studies of the brain established degenerative and inflammatory variations. The presence of intranuclear incorporations is not sufficiently visible.

IMMUNITY. A repeated infection of an animal has not been noted. In horses, recovering after encephalitis, the quantity of antibodies neutralizing the virus is increased. Effective means of treatment are negative. In the USA a vaccine from chicken embryos is used for immunization of horses and mules. The best results are obtained during application of the vaccine two weeks before the outbreaks of the disease.

By method of ultra-centrifugation it was established that the size of the virus is 20-25 microns. The virus, the eastern as well as the western, is well preserved in 50% glycerin under pH 7.4 and in an acid medium at pH 6.0; in a more acidic medium it is disrupted very quickly. The virus is also disrupted very quickly in formaline and caustic soda; the virus is stable to 0.5% phenol. In a frozen or dried state the virus does not lose biological activeness for a year.

X-DISEASE(Secondary infection). In American literature, descriptions of an unknown disease of horses, which is characterized clinically by intensive icterus, atony of the bowels, retardment of urine, absence or presence of a low fever and nervous symptoms before a sharply expressed excitation, are encountered more and more often. Haemoglobinuria is sometimes noted during this disease. Grown horses are mainly affected. The outbreaks of this disease develop 5-6 weeks after an enzootic of IBV. The course is acute, death results in 24-48 hours. During dissection there is ascertained an intensive generalized icterus, dehydration of the organism. The liver is enlarged, friable, with appearances of parenchymatous degeneration. The kidneys are sometimes enlarged, often with petechia. The spleen is often enlarged. The small intestine is hemorrhaged.

During histological study of the brain, no variations were noted. In the liver there is constantly noted a parenchymatous degeneration with necrosis in the lobules and infiltration of the cells, but in the brain, only parenchymatous degeneration. Attempts to isolate the virus were unsuccessful, therefore some authors suggest naming the disease 'a toxic hepatogenic icterus' others - 'X-disease' 'toxic encephalitis'. A medicinal-prophylactic measure has not been developed. The serum of recovered animals was used as a treatment of the x-disease. The results were negative.

INFECTIOUS ENCEPHALOMYELITIS of horses in the USSR. The etiology of IEM of horses was first established in 1932 by S. N. Veshelesski and I. G. Levenberg. In the following years the agent of IEM was obtained by other researchers also.

The obtainment of the virus from fallen animals is very difficult. From the moment the virus nature of this disease was established there have been many attempts to develop a method which would allow for a more constant, or at least a more often isolation of the virus from the brain of horses which have fallen under natural conditions, with a clinical chart of IEM.

In 1944 G. K. Ishukov and V. I. Yakushev reported that they were able to obtain the virus more often by preliminarily cultivating the material on 10 day chicken embryos than by the ordinary direct infection of rabbits with a brain suspension prepared from the brain of a horse fallen from IEM.

In 1943 the following method was developed for the isolation of the virus of IEM of horses. The brain of the fallen horse was subjected to a six-fold freezing in a period of 3-5 days, then a suspension was prepared from it and intracerebrally injected into rabbits. By this method it was possible to obtain 20 strains of the virus of IEM.

During the studies of the strain characteristics of the virus of IEM which had been isolated by many authors, it was established that the most

susceptable animals to IEM are horses, rabbits, white rats, hares, hedgehogs and white mice. These animals always become ill during inoculation of the virus intracerebrally, intranervally, subdurally, and sometimes during introduction of it with liquid, and not always during the introduction of the virus into a deep strata of the muscles of the lumbar region... (Shoenbat, 1940).

In 1944 Y. E. Kolyakov and A. M. Romanov caused infection with IEM in 30 rabbits by means of a sub-lingual inoculation of the virus. After the infection of the virus into the under-tongue region the authors noted the development of a clear clinical chart of IEM in many of the rabbits. During histological study of material of several rabbits, there was established a non-ulcerous encephalitis (L. M. Pichugin).

It is seldom possible to cause infection in horses and rabbits by the intravenous introduction of the virus-brain. Dogs and guinea pigs are less susceptible to this virus. Chickens, poults and sparrows are not susceptible to this virus.

The lethal dose for susceptible animals, during intracerebral and other methods of infection, are not alike. It depends on the condition of the medium and length of storage of the pathological material. The lethal dose of virus-brain for horses during suboccipital infection fluctuates from 0.75 (strains 17.50 and H2) to 2.5 g (strains 392, 66-u and H2), and for rabbits, during intracerebral infection, from 0.0008 to 0.0015 g.

It is recommended that the brain, stored no more than 5 days, be used for the determination of the biological characteristics of the virus.

The first data on the virus isolated by the Soviet authors were incomplete and led to the identification of the virus as one of the Borna (Fridman and others). Further, deeper works established that the agent

of the Borna disease is different by immunological properties, as well as by its peculiar pathomorphological variation which are constantly observed in fallen animals in the nervous system. Characteristic for the Borna disease is the presence, in naturally fallen and experimentally infected animals, of a non-ulcerous encephalitis and an intranuclear incorporation in the nuclei of the ganglion cells (Joest and Sogen bodies).

In certain regions of the Far East there is an encephalitis of horses which is described as different from the ordinary encephalitis by its characteristic course, serological peculiarities and morphological variations.

In pathological material from horses fallen, with signs of affection of the central nervous system in the territory of the Far East, S. M. Vorontsov and Sidorov described the variations which, by their character, are similar to the variations during the Borna disease. S. T. Ryagin reported on the isolation of a virus, by him, in the Far East, from a horse sick with encephalomyelitis, which by its biological properties differed from the strains of virus of IEM which are isolated from horses in other points of the Soviet Union.

On the basis of the above data it is possible to think that in certain regions of the USSR an encephalitis, of a diverse origin is being encountered in horses. These data have a practical significance for the further accumulation of clinical and epizootological material, and mainly for the development of a method of treatment, measure of combat and prophylactic.

The virus isolated in the USSR territory differs from the American (eastern and western) mainly according to its smaller circle of susceptible animals and birds and non-susceptibility of man, shorter period of illness, greater stability of guinea pigs, greater diapason stability in an acid medium (pH 4.5); the size of the American virus is about 25-30 microns, The Russian, according to I. A. Shmanenkova, 80-120 microns.

Cross immunization and a method of serological studies established a concise difference between the Borna and American eastern and western and the virus isolated in the USSR (Shcherbatekh).

S. M. Veshelesski and co-workers, while studying the biological and serological peculiarities of viruses No. 2 and 6, noted a similarity of these viruses according to pathogenicity for numerous small test animals, virucidal action of specific hyperimmune serums of horses, as well as in cross immune reactions.

P. Ya. Shcherbatekh, A. A. Levashov and M. P. Serov (1944) established a distinction between the agent of IEM of horses and the virus of rabies, by cross infection of horses and by a method of neutralization of the virus by hyperimmune serums.

Strains of the virus of IEM of horses, isolated in various sections of the Soviet Union, are similar according to their immunological and serological characteristics. But, there are several differences among the separate strains in regard to virulence to various animals, and other lesser ones. Thus, a part of the strains causes infection in white mice, and part of them does not possess these properties. Also noted was the fact that not all the strains possess the properties necessary to adapt themselves on chicken embryos.

Of 12 studied strains, the most virulent are strains 50, 17 and H2. During this it was established that the virulence of the strain does not depend on the antiquity of its isolation. Thus, strains H1 and 66-u were isolated 4 and 2 years ago, and their virulence is significantly weaker than that of strains 50 and 17, which were isolated more than ten years ago. Strain 392 is equal to strains 17 and 50 according to the length of lab storage, its virulence is almost identical with strains 66-u and H1.

V. I. Kutovin studied the biological properties of strains No. 2 and 6 of IEM of horses, filterability of the virus through the Chamberlan L2

and L3 filters, Berkefeld V and W and Zeitzsa filters. The size of the virus particles of IEM are determined by filtration.

I. Ya. Shcherbatskh and B. V. Sidorenko reported that ordinary methods of filtration of virulent suspensions of brain do not always afford establishment of the presence of virus in the filtrate. During the application of the extraction method in weak alkaline solutions (0.01% NaOH), with two-three-fold preliminary freezings at 8-10 C, it is always possible to obtain positive results; 0.1 ml of filtrate from a brain emulsion, prepared on a physiological solution in dilutions of 1:40 and 1:80, caused death in rabbits in that same period^{or} when the control rabbits were infected with the original ~~non~~non-filtered suspension.

STABILITY of the virus. It was established that solutions of 5% chloride of lime, 5% phenol, 0.2% formaline and 2% creolin render a 20% virus suspension harmless in 10 minutes. 1% of a heated (60 C) solution of creolin renders a suspension of brain virus harmless in 3 minutes, a 2% solution of chloroform in 1 hour. Virus-brain in 30% glycerine loses its virulence in 3 months storage. Direct sun rays, acting on a brain suspension in a dilution of 1:20, room temperature of 24 C and a layer 2.5mm thick, inactivate the virus in 6-8 hours. Ultraviolet rays render a 20% solution of suspension harmless in 5 minutes, a layering of 2mm (source of light at 75cm).

The photodynamic action of methylene blue on a suspension of virus^o brain was noted by Matovin and Ishukov. According to these authors the virus of IEM, in a suspension status 1:40, is inactivated by methylene blue in dilutions of 1:40 000 in 30-40 minutes under artificial light, under irradiation of direct sun rays in 10-15 minutes. On the basis of these data, photovaccine was suggested for the battle with IEM. It was established that the virus of IEM is very labile to high temperatures.

A suspension of virus-brain, prepared on a physiological solution in a dilution of 1:20, is rendered harmless by heating to 50 C for 10

minutes, during boiling- in 1-2 minutes. Freezing at minus 60 C, followed by thawing(1-2 hours), does not render the virus of IEM of horses harmless. According to L. S. Ratner, the virus of IEM is stable to the continu action of very low temperatures (minus 180 C).

The virus proved to be no less stable to drying. According to Shcherbachev and Sidorenko, a virus-brain, dried in a vacuum at 14-18 C to an 0.4% remainder of moisture, remains virulent for 54 months.

In view of the fact that the virus of IEM of horses is stable to low temperatures and labile to high, it would be well to disinfect buildings, equipment and articles of maintenance with solutions of creolin, caustic soda, carbolic acid or by heating to 60-80 C.

EPIDEMIOLOGICAL DATA. Infectious encephalomyelitis of horses usually progresses as an enzootic of sporadic cases and very seldom as an epizootic.

The IEM disease of horses is encountered in forest and swampy, in steppes and mountain areas. Its appearance is not connected with any characteristic of the pastures or watersources. However, most often the horses which located in herds and work on agricultural lands become ill, this indicates the possibility of transmission of this disease by the blood-sucking insects. There have been noted cases of infection of horses in city usage during stable sheltering. Makarove observed cases of infection of horses which were working in mines.

IEM of horses is regarded as a seasonal disease, and appears most often in late spring and in the summer-fall time. The start of the infections is noted in May-July. The maximum infection rate is in July-Sep. Separate, seldom observed enzootic outbreaks in winter have been described.

There are data which point to the intensity of the enzootic IEM of horses in the first 2-3 decades of the outbreak of the disease. Besides this, there is another course of the enzootic, more equal. In this case

the infection of animals is almost daily for 3-4 weeks and more, then it terminates. Shcherbatekh, continually observing the course of the enzootic of IEM of horses, noted that it repeated itself in a determined area after 2-3 years, less often after longer periods of time. In some areas the IEM was observed for 2-3 years in succession. The intensity of the enzootic in the latter case was very weak, and in certain isolated areas, only sporadic cases were noted during this period of time. The different courses of IEM of horses in for a single area has not as yet been connected with the number of biting insects. It has been noted that in the spring of those years when the intensity of the enzootic was greatest, there was more precipitation than in the springs of better years. This peculiarity could, indirectly/ at least/, indicate that the greater amount of precipitation stipulates the formation of biotopes in the spring months. The enzootic outbreak of IEM is sometimes preceded by one or two sporadic cases, so called forerunners, then after 2-3 weeks the enzootic develops.

In the accounts of one veterinary commission (1943) there were data on the increase of the infection rate of IEM and length of interval between the cases of new infections. From this there were established 3 types of courses of enzootic IEM of horses:

- 1) closely grouped, that is, daily or almost daily new infections over a long period of time;
- 2) interval- infections with more or less significant intervals (days, week, etc);
- 3) grouped-interval course, that is, a combination of grouped and interval appearances of new infections.

According to this same commission, in stables, where the rate of infection was most expansive, there was a closely grouped course. During the grouped-interval course the damage was less than during the closely

grouped course. The least number of victims was accounted for in the stables during the epizootic of an interval course."

Most often there is an abrupt dying-away of the enzootic, less often a lengthy one. During a lengthy termination of an enzootic the number of new cases is increased very 1-38 days. This indicates that the infection does not terminate, but continues to 'warm itself' in the area.

The death rate is high during IEM. In the beginning and at the height of the enzootic the death rate is higher than during the termination.

SOURCES OF infection and PATHS of natural infection. As yet there are no proven data which would reveal the tying link between the infectable animals and the possible reservoir of the virus in nature. It is ascertained that the virus of IEM of horses is retained in the organism of mammals; in the warm period of the year the virus can be transmitted by various hematophagia and ticks to the basic host- the horse. The ailing horse becomes the basic source of infection for the healthy animals.

This assumption is confirmed by the seasonality of the disease, with the maximum intensity of the enzootic in the summer-fall period, and also by experimental data which were obtained on test animals. The separate enzootic outbreaks in the winter time cannot disprove the above point. The winter outbreaks need more accurate study. With this we should try to decide the possibility of the virus being retained by the rodents which inhabit the hay and strawstacks. No establishment has been made on the importance of the ectoparasites, particularly lice, in the transmission of the virus of IEM. Attempts to detect the virus in mosquitoes, caught in the centers affected by IEM, as yet have not given positive results. Attempts on the direct transmission of the virus of IEM were almost always successful.

At the present time the question of transmission of the virus of IEM in experimental conditions ~~cannot~~ be considered solved.

A. P. Murashov and Dedova (1939) obtained positive results during experimental infection of animals by means of transmitting the virus by the *Aedes cinereus* mosquitoes.

Analogical data were obtained by P. G. Sergeev and A. K. Shubladze (1954). These authors established the transmission of the virus of IEM on small animals by the mosquito '*Culex pipiens*'.

G. K. Ishukov, F. A. Ishukova and E. M. Emchuk experimentally infected the '*Dermacentor marginatus*' ticks with the virus of IEM. This led the authors to express the idea that, in stationary affected points, the *Dermacentor* ticks can be spontaneously infected by the virus of IEM. O. Vasilev (1947) obtained similar data.

There also are reports on the transmission of the virus by the stable fly (*Stomoxys calcitrans*) (Bartsevich).

P. L. Petrishcheva and E. N. Levkovich isolated four strains of virus from the ticks '*Hyalomma anatolicum*, *O. laghorensis* and *O. papillipes*'. During typification of these strains, they were regarded as virus of IEM of horses. On the basis of the obtained data the authors consider that both types of ticks are vectors of the virus of IEM of horses.

F. Z. Amfiteatsov noted, on the basis of an analysis of epizootological data (1941), that the IEM of horses is observed more often in those zones where the tick-vectors of the hemosporidium exist than in those zones where the tick does not exist.

The separate outbreaks of IEM in the winter season indicate the necessity of clarifying the role of the ectoparasites and rodents in the dissemination of the virus of IEM of horses.

The possibility of infection by contact is very doubtful. There are only several indirect indications that such an infection, as the infection of a horse by application of large doses of virus on the scarified mucous

membranes of the nose, being possible (N. A. Romanov, P. Ya. Shcherbatekh). However, in tests of Shcherbatekh (1939), a lengthy (50 days) herding of healthy, ailing and recovering animals together in a pasture and pen did not stipulate the infection of the healthy animals. The test included 12 healthy, 9 ailing and 7 recovering horses. Data on the localization of the infection in the central nervous system indicate the impossibility of a contact infection, as well as the negative results of artificial infection of horses and rabbits by introduction of large doses of the virus of IEM through the food tract. Infection of rabbits with filtrates of urine and saliva gave negative results, which also indicate the slight possibility of infecting horses with IEM by contact.

PATHOGENESIS. The pathogenic action of the virus of IEM causes affection of the central nervous system, which in its turn stipulates disruption of the activity and volume of substances of the complete organism. The virus, entering the organism, reaches the central nervous system along the nerve stems, causes an excitation in the cortex and substantia grisea ganglion which is displayed in the complicated reactions, according to signs and strength, of the ailing organism.

The irritation, penetrating into the cortex directly under the influence of the virus, or reflectively through the extero-intero-receptive connections, inevitably influences the adjacent sections of the nervous system, and first of all, the hypothalamus region, which plays a vital role in all functions of the organism.

A specific agitation, penetrating the cortex, causes disruption of the coordination of the intero- and extero-receptors, disruption of the function of the organism, which is accompanied by the appearances of dystrophic processes.

Significant dystrophic variations take place mainly in the liver and kidneys. In the other organs the variations are expressed less.

Pathological processes, penetrating the cortex under the influence of a specific agent, stipulate a self-styled IEM of horses clinical chart, the character of which is determined by the degree of irritation of the central nervous system and depends on the condition of the animals, their age, fatness and conditions of stables(pens, etc).

I. P. Pavlov considered the pathological process as a determined reaction of the organism to the action of a specific irritation in known conditions. He credited a significant role in the pathological process to the receptor apparatus- peripheric endings of the centripetal nerves. I. P. Pavlov said: "It seems evident that in the life of a complicated organism the reflex is the most essential and most often nervous appearance. With their help the correct and exact relation of sections of an organism is established among themselves and in relation to the surrounding conditions. The originating point of the reflex is the irritation of the peripheric endings of the centripetal nerves. These terminations penetrate all the organs and their tissues. These endings must be considered as extremely diverse, specific, similar to the endings of the nerves of feeling, adapted each to its own irritation of a mechanical, physical or chemical character or formation. A degree of their work in each moment determines the size and combination of the activity of the organism". Besides this Pavlov pointed out that:

"...extraordinary irritations, appearing as morbidic causes, represent specific irritations of those protective apparatuses of an organism which are assigned to battle the respective causes.

We think that this representation should be generalized for all cases, and in this we have the general mechanism of adaption of the organism in general, during encounters with pathogenic conditions which are similar to the normal irritations and adaptations in the way of life, which have specific irritations for one or another apparatus."

Thus, Pavlov stressed the special significance of the receptor apparatuses in all life processes of the organism, in particular in its responsive reaction to the introduction of specific agents of infection.

During IEM of horses the virus, as indicated above, is the specific agent, the nature of which, to the present time, is insufficiently studied, but many of its peculiarities are known.

At one time the opinion existed that infection of horses was possible only intracerebrally or suboccipitally. At the present time there are data which allow using conditions in tests which are similar to the natural conditions of infection. It has been established that the introduction of the virus into any nerve stem or any branch of it, and also into the muscles of the adrenal region, rich with nerve endings, directly emanating from the spinal cord, causes infection in horses. This indicates the specific electivity (affinity) of the virus of IEM to the nerve tissue, and is confirmed by the fact that an intravenous introduction of 30-40 deadly doses of virus-brain caused infection in limited cases, and the introduction of the virus directly into the lymphatic ganglion causes infection.

Besides this, the constant detection of the virus of IEM of horses only in the tissues of the central nervous system indicates another peculiarity—the ability to develop in brain tissue. Results of tests by P. Ya. Chcherbatekh and S. B. Logginov give proof of the ability of the virus to multiply in brain tissue. This was done by injecting horses with 30 lethal doses of virus of IEM through an occipital pin-hole, and after various periods of time they took serum and studied it for the presence of the agent. It was established that the liquor of horses, infected thusly with virus of IEM, does not contain virus. Samples of liquid taken after 4 minutes, and also other samples, taken at various intervals until the death of the horse, caused no infection during intracerebral introduction,

in rabbits

a suspension of brain from a horse infected through an occipital pin-hole, then killed after 6 hours, contained virus; rabbits infected with this suspension became infected with IEM.

The elective characteristics of the virus of IEM and its ability to be fixated by the nerve endings are confirmed in other work.

Multiple introductions of small, and single introductions of large doses, into places with less developed nervous systems, do not stipulate the development of an infectious process. Similar data, noted by A. D. Speranski and D. P. Pletsit, were evident during a study of tetanus toxin. The authors established that the place of injection of the toxin has an important meaning in the reproduction of the tetanus. Thus, the intramuscular introduction in the region of the extremities is taken 10 times smaller than during intravenous application.

The above data allows the assumption that in natural conditions the virus of IEM, entering an organism, does not always cause infection.

On the basis of the above data it is possible to say that, in natural conditions the virus of IEM, entering the central nervous system, causes a pathological process in it. A direct inclusion into the pathological process of the nervous system stipulates an acute, and often very acute course of infection, often causing death in 1-2 days.

In the initial period of the infection process there appear in the ailing horses signs of depression, jawing, hyperkinesia of the lips and drowsiness. With the development of the disease there is a limited weakening of the skin, hair and knee reflexes, and followed by the anal reflex. As a result of the development of the pathological process in the central nervous system there is a disruption of the coordination of movement in the ailing horse, hyperkinesia appears, the gait becomes staggered, the animal moves in circles, irrepressibly rushes forward.

The disruption of the reflector activity in the horse causes disruption of the functions of almost all the organs, and especially the liver. The tissues of the liver lose the ability to process the products which enter it from the disintegration of the blood, this leads to the accumulation of large quantities of bilirubin in the blood and the icteric coloration of the mucous membranes, subcutaneous cellular tissue and several other organs.

The appearance of bilirubin in the blood is ordinarily noted somewhat earlier, or simultaneously with the ictericity of the sclera and mucous membranes of the eyes. The affection of the central nervous system attracts a disruption of the activity of the parasympathetic and sympathetic systems, which leads to the appearance of paresis of the gastro-intestinal tract and bladder. As a result of the paresis there is a termination of the digestive action, peristalsis and urination. Specific effects, causing a stable irritation of the central nervous system, lead the animal to an excitative state which is accompanied by increased muscle work and abundant perspiration, and stipulates the disruption of the water volume and loss of weight.

With the appearance of paresis of the muscles of the glottis, tongue and lips, the animal is not in condition to drink water. As a result of the great loss of water, due to increased muscle action, perspiration and inability to replenish the supply, there is always noted a dryness of all the mucous membranes which contain the stomach and intestines in the organism of the horse ailing with IEM. In the gastro-intestinal tract there originate congested phenomena which, in their turn, lead to the decay of the contents of the stomach and intestines, with the formation of toxic products.

Non-specific toxins, being absorbed and entering the blood, act on the entire organism and increase the disruption of the liver even more.

and the disruption of its barrier and processing functions render a severe disruptive action on the kidneys, in which there is always a granular degenerative action on the epithelium of the uriniferous tubuli and serous glomerulonephritis. Variations take place in the heart and other organs also.

Variations are abruptly indicated in the blood. There is a respective increase noted in the number of erythrocytes (by 1 1/2 times), leukocytes by 2-3 times. There is a true increase in the number of red and white blood cells at the beginning of the illness, only because of the increased production of them, then, as a result of the condensation of the blood, this increase is relative.

In horses with IEM there is always a slowing of the sedimentation of erythrocytes noted. It has been experimentally proven that this phenomenon is stipulated by the accumulation of bile in the blood, which causes disruption of the electrical conductivity of the erythrocytes, and also condensation of the blood, which is caused by dehydration of the organism.

The presence of disrupted erythrocytes is often noted. There is a significant decrease in the number of them. The reason for such a decrease is as yet unknown, but the very fact of aneosinophilia is an unsuitable prognostic sign. The number of monocytes fully decreases, and this indicates the weakening of the protective properties of the organism and the oppression of the function of the reticuloendothelial system.

Significant variations in the structure of the neutrophils are noted, the nuclei of which are degenerated with sharply segmentated signs; the protoplasm is friable, with great quantities of granular inclusions.

In the lymphocytes there are always observed variations of the nuclei and friability of the protoplasm. Significant changes take place in the bone marrow also.

While studying the cells of the bone marrow of horses with IEM I. G. Pyanikov noted that the myeloblastic group of cells was not increased, but young (juvenile) forms, in stages of sharply expressed degeneration, were predominant in it. The quantity of histiocytic and monocytic cells was increased noticeably.

The variations in the blood and bone marrow indicate the distortion of the blood-creating function as a result of the disruption of the reflector activity and general intoxication of the organism. Under the influence of these causes there are changes in the walls of the blood vessels, accompanied by numerous hemorrhages in the brain and spinal cord, parenchymatous organs, mucous membranes of the gastro-intestinal tract, bladder and in the lymphatic ganglion.

The dehydration of the organism, the disruption of the metabolic and acidifying processes, in the long run, lead to an abruptly expressed acidosis and anoxemia. The amount of lactate acid in the blood is increased by 1 1/2 times, the quantity of potassium, calcium and sodium chloride is decreased. The carbohydrate volume is disrupted; and an abruptly expressed glycemia emerges. The reserve alkalinity of the blood is lowered; pH of the blood reaches 6.8.

As a result of the affection of the nervous system and the increased muscle activity, there is a disruption of the heat volume, by the end of the illness the temperature of the body is below normal.

With the improvement of the condition of the ailing horse there is a respectively quick restoration of the activity of the greater hemispheres to normal, and also of the extero- and intero-receptors.

With the restoration of the functions of the central nervous system there is a fading of the nervous excitation of the ailing horse, but the oppression remains for some time.

All this indicates that the central nervous system, in particular the cortex of the brain, during a weakening of the action of, or full absence of a specific irritation possesses the ability to quickly restore the reflector activity of the organism while the variations in the other organs remain.

After a clinical improvement in the ailing horse there are noted pathological appearances in the various organs, tissues of it, etc. for some time. Thus, morphological variations in the liver are noted for 40 days and more after the clinical improvement of the animal, which is confirmed by biopsy of the liver and the detection on the 25th day of an increased quantity of bilirubin in the serum of blood of recovered horses.

Albumen remains in the urine of the recovered horses for 15-18 days. In the white blood there are detected pathological cells, mainly of the neutrophil group. These appearances indicate the residual variations in the liver and hematopoietic system, and require an accurate and lengthy observation of the clinical recovery of the horse.

In case of an adverse course of infection the pathological processes in the ailing horse develop very quickly and are accompanied by sharply expressed irreversible variations of a dystrophic character, leading to death. Death results from an abrupt disruption of the activity of the central nervous system, catastrophic decomposition of the albumen, anoxemia and paralysis of the heart.

COURSE OF ILLNESS. The incubation period during natural infection has not been exactly established; on the basis of the epizootological data it is considered to be 40 days. The course of the illness in an absolute majority of the horses is very acute. According to the reports of various

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authors 78-82% of the horses die in 24-48 hours. During a lethal beginning the disease in 97% of the cases lasts from one and one-half to ten, and only in certain cases to 16 days.

The prodromal period during IEM of horses is very short—from several hours to one day, less seldom 3-5 days. In this time the horses are sluggish, fatigue easily, move with a lowered head, their appetite is decreased.

The appearance of a nervous syndrome is regarded as one of the early clinical signs, it indicates affection of the nervous system. The horses experience a disruption of sensitivity, they involuntarily jerk their lips, do chewing and suctioning movements with their mouth, shake their head, sometimes raise it. A twitching of certain muscles appears and there is an increase of perspiration on certain sections of the body. The coordination of movement is disrupted. With the development of the disease the nervous appearances increase, but not in the same degree. There appears an irritational icterus. The icterus of the mucous membranes grows during the entire course of the infection, its decrease is coincidental with the termination of the activity of the digestive tract.

With the full absence of peristaltics there is observed an extensively large quantity of bilirubin. There is a smaller quantity of bilirubin noted during an incomplete termination of the peristaltics in the ailing horse. Most often of all the first appearances are the nervous appearances, then the icterus of the mucous membranes and weakening of the activity of the gastro-intestinal tract. Irregardless of the quick course of the illness, a majority of the horses become gaunt, this indicates the disruption of the metabolism and significant dehydration of the organism in connection with the increased perspiration.

The parietic appearances are registered later than the hyperkinesis. Paresis of the intestines, masticating muscles and lips and extremities are most common, less often with the tail. According to Shcherbatskh,

of 62 horses with full paresis of the gastro-intestinal tract, 44 fell; of 39 horses with incomplete paresis, that is, with a weakening of this tract, 11 fell. The reflector activity is weakened or reduced to a minimum. The sensitivity of the skin is somewhat lowered, the iliac, knee and hair reflexes are gradually faded, especially in the terminating stage of the illness. The ear and anal reflexes fade later; a significant weakening of them indicates the severity of the disease.

Locomotive disruptions and a breakdown of the coordinations are noted. They appear in the staggered gait and in the movement of the legs without bending of the knees, they usually remain the entire illness. Ailing horses suddenly stop, stand for sometime with legs far apart and with the head almost to the ground, they attempt to move forward without going around obstacles, as if blind; sometimes they involuntarily move in circles. Standing in position, the ailing horses often lean their head towards the ground or cock it to one side, during the presence of a support they maintain their head in any position. An unexpected fall is accompanied by an attempt to rise, this causes the animal to assume the pose of a sitting dog. Laying on its side the horse makes swimming movements and rears its head back to its spine.

During the entire illness there is observed a fascial tremor and a jerking of the muscles of the shoulder area, chest, neck, lumbar region and, less often, the peritoneal walls. A blow from a blunt or percussion hammer, in a majority of the ailing animals, might cause a temporary curtailment of the jerking.

Another indication of the disruption of the nervous system, mainly the cortex of the brain, is the hypostesis of the skin, paresis of the action of swallowing, partial or full loss of sight, retainment of urine

at the height of the illness and the involuntary urination in the terminating period of the illness.

All the enumerated signs appear very fast. There has also been noted a loss or fading of some signs.

In an absolute majority of the ailing horses breathing becomes more difficult at the height of the illness, the number of breathing movements reaches 40 per minute, and in certain cases-50-60.

At the termination of the disease the breathing becomes deeper and slower. In the period of fading, almost a deep sleep, the breathing remains normal, often interrupted by deep inhalations.

In horses ailing with IEM there is constantly observed an increased perspiration, even on those areas which are dry under extremely hard laboring of a healthy animal.

The dryness of all the mucous membranes, evidently, is connected with the significant dehydration of the organism, this disrupts the metabolism and heat-regulation of the ailing organism.

Of 144 horses under our observation, only 12 animals had a saliva discharge, mainly in the beginning of the illness, this differs from the rabies disease, which is accompanied by salivation and ends with death for all those infected.

The percentage of recoveries from IEM, particularly if treatment is applied immediately, can be high. In a majority of the ailing animals the break-through to recovery is most often on the 3rd to 4th day.

During recovery the first appearance is peristaltics, then restoration of sensitivity and reflector activity. Some of the symptoms fade slowly. The icterus often lasts for a long time, from 10-12 days.

Dividing IEM into a violent or quiet form according to clinical appearances is quite conditional; only one or another sign can be noted

as being predominant. Most often there is an alternation of the depressive status with the excitation. These vary in intensity.

THE HEMATOLOGICAL variations in the ailing horses are very characteristic. A devoted study of these changes proves very helpful in diagnosis.

With the appearance of the clinical signs there is observed an increase in the number of erythrocytes and bilirubin. At the height of the illness the number of leukocytes is increased to 13-16 thousand (sometimes to 26). There is an expressed degenerative 'shift to the left' of the neutrophils. The number of bacillary-nuclei cells reaches 8-12, less often 18-20 %; There is also an increase of the number of myelocytes and immature forms. As soon as the first few hours of infection there is noted a decrease of the number of eosinophils and lymphocytes. After 8-10 days the number of eosinophils reaches 6%, the lymphocytes-45%. The degenerative forms of neutrophils in the hemograms of recovered horses is encountered in 15-18 days. In some recovered horses the eosinophils and lymphocytes remain for some time (1-2 months).

The quantity of bilirubin in horses ailing with IEM is fluctuant from 10-90 units, by determination according to Meilengrakht. The increase of the quantity of bilirubin accompanies the appearance of icterus on the mucous membranes. The clearer the icterus is expressed, the more the detectable the bilirubin is in the blood.

In healthy animals the quantity of bilirubin is 8-12 units. The speed of the increase of the quantity of bilirubin, and also the degree of its indicator are orientations of the severity of the course of infection. The increased quantity of bilirubin was noted 18-20 days after the noted recovery.

The ESR in ailing horses is slower. In 40% of the victims the erythrocytes settled in the first 15 minutes from 0 to 10 divisions, in one hour-15-18 divisions. In 35% of the ailing horses the erythrocytes settled in

15 minutes from 5 to 18 divisions, and in an hour-20-25 divisions. In 2.2% there was an insignificant hinderance of the ESR. Of 31 horses with an E. S. R. of 0-10, 29 fell; of 19 horses, with 15-30 divisions in 15 minutes, 7 fell(Shcherbatekh). Consequently the indicators of the ESR can serve as a prognostic sign and can be utilized for control during testing of new therapeutic measures.

COMPLICATIONS and their character. The residual phenomena, besides variations in the blood, are noted very often in recovered horses. Two cases are described where there was affection of the nervous system. Thus, in horse No. 419, three years old, after recovery there was a disruption of the innervation of the shoulder muscle with a successive decrease of it. After 60 days the sensitivity of this muscle appeared again and then the innervation was restored. In a 4 year old mare, No. 811, in 45 days there was a disruption of the swallowing action. The animal was feed artificially during its illness.

In ailing or recovered horses, in some localities, there is a photodynamic action by the sun rays on the un-pigmented sections of the skin observed, mainly on the extremities and bridge of the nose. In the horses there are noted hyperemia, loss of elasticity(parchmentation), swelling and followed by necrosis of the skin(after 6-8 days), then the entire necrosized area tears away like a thin crust. The sections, deprived of the skin, heal slowly. As a prophylactic we smeared the respective sections of skin with tar, once every three days. This significantly lowered the appearances of the photodynamic effect.

PATHEOLOGOANATOMICAL and HISTOLOGICAL variations in the horses fallen from IEM are almost identical.

Examination of the fallen horse usually discloses icterus of the subcutaneous cellular tissue, mucous and serous integument, often of the liver.

The conjunctives and the subcutaneous cellular tissues are intensively tinted a yellow color, more than the mucous mouth and nasal cavities and digestive tract.

Almost all the organs show signs of hemorrhages. They are from fine-dotted to striated and circular. The hemorrhages are always found under the mucous of the bladder, gastro-intestinal tract, on the heart and nasal bridge. Necrosis is often found on the latter. On other sections the hemorrhages under the mucous and serous membranes are not constant.

In a majority of the cases the stomach is somewhat enlarged in volume, over-filled with a great quantity of dry, often compressed food masses which have an acidic type odor; analogic appearances are significantly less often observed in the large intestine. The walls of the stomach are expanded, thinner. The mucous membranes, as a rule, are sharply hyperemiated, on the hyperemiated sections there are small ulcerations. Often it is covered with a viscous, grayish mucus (catarrhal gastritis). Somewhat less often analogical variations are observed in the rectum. The walls of the small intestines are often swelled, under the mucous there are hemorrhages, in places forming hemorrhagic inflammations, some places 5-10-35 cm.

The liver is usually decreased in volume, limp, with tapered edges. The pattern on the cutting is particolored, with yellowish, less often with yellowish-brown tints. In numerous cases there is a mosaic pattern. After fixation of a piece of liver in formaline, the fixating fluid is tinted a greenish color. Sometimes smaller serous spots are observed on the cutting.

The lymphatic nodes are slightly varied. The pancreas are enlarged and sharply icteric.

Other organs are subjected to variation less regularly. The most characteristic are the enlargement of the heart, limpness of its muscles and presence of inter-muscular hemorrhages. The skeleton muscles are limp,

the tendons icterus. The intermuscular layers are seriously infiltrated. The degree of intensity of these variations are in direct conjunction with the course of the illness.

The histological variations in the organs of the horses which have fallen from IEM are typical, particularly in the liver. In an absolute majority of the cases there are clearly expressed dystrophic variations and degenerative adiposity of the liver cells.

The 'stringer' structure of the cells is disrupted. The cells of the liver are without structure, many of them isolated. In the interlobulate tissues, and also in the center of the lobules, there is a retention of infiltrate. These variations are so typical that they serve as the basis for establishing a diagnosis.

The spleen is shrunken or without definite variations, upon dissection it is dry, solid, or over-filled with blood. There is noted a decrease of the hemosiderin in it during histological examination.

In the kidneys of a majority of the fallen animals there are congested variations and a cloudy swelling of the epithelium of the convoluted tubules. In numerous cases the variations in the kidneys are almost un-noticable.

In the brain the variations are constant, but not strictly specific. Most often there is an expressed hyperemia of the vessels, less often edema. In approximately 90% of the cases small punctate hemorrhages are present in all the sections of the brain, also hemorrhaging in the spinal cord.

According to the data of one veterinary commission(1943), during the examination of 40 brain specimens, hemorrhaging was established in 21 cases. P. P. Pirog, while studying the brain from 20 animals, fallen from IEM, noted hemorrhaging in 12 cases.

B. G. Ivanov and D. A. Priselkova determine the variations in the central nervous system as degenerative processes and only in separate cases as an inflammation. Pireg, during examination of a number of horses having fallen from IEM under natural conditions of infection, did not detect an inflammatory appearance in any of the brains.

DIAGNOSIS for IEM is based on the detection of a clinical chart for horses, this includes affection of the nervous system in conjunction with icterus of all the visible mucous membranes and atonia of the gastrointestinal tract.

A pathological dissection, in particular a histological examination of the brain of fallen animals, has an essential importance for the establishment of an initial diagnosis, and in successive cases- for the confirmation of the diagnosis.

Soviet scientists (Zotov, 1948; Shcherbatekh, Sidorenko, Syagaev, 1948; M. V. Revo and K. V. Shtaly, 1949; Ryagin, 1949) applied the CFT method of analysing the serum of ailing and recovered animals. This method has an important significance in a differential diagnosis of various encephalides and food poisoning (Shcherbatekh, Sidorenko).

An early diagnosis of the infection of horses with IEM by the presence of an increased quantity of bilirubin in the blood proved itself not worthwhile. However, the determination of the content of bilirubin in the blood of ailing horses along with an ESR and an enumeration of the hemograms can be used for the diagnostic purposes. A retarded ESR and an increased quantity of bilirubin do not serve as specific indicators of an IEM infection, but with other data and with the presence of a characteristic clinical chart they simplify the diagnosis.

Exact method of diagnosing early or concealed forms of IEM of horse have not as yet been developed.

The biological method of diagnosing for IEM on lab animal, because it is complicated and lengthy, has not receive any great practical application, but can be used to exclude rabies.

DIFFERENTIAL diagnosis has been developed quite clearly. A great interest in in the differentiation of IEM from rabies. During rabies the characteristics of the disease are bites, lengthy salivation, intense excitation and unrest. Rabies passes with an increased temperature, only in the last days does it drop to 35-36 C. The duration of the illness is varied, an average of 6-8 days. Death rate-100%. Sensitivity at the locale of the bite is increased. An aggressiveness towards animals and man is noted, also paralysis of the deglutitory muscles and back(tail). There is an absence of icterus of the visible mucous membranes. The atonia of the gastro-intestinal tract is weakly expressed. A histological examination usually discloses Negri corpuscles(bodies) in the ganglion cells of the brain.

THE BORNA disease differs mainly by its peculiar histological variations in the central nervous system (presence of Joest bodies), duration of course(10-14 days) and several epizootological peculiarities (registered in May-June, and IEM in summer-fall period).

SECONDARY encephalides are encountered during hematologic-parasitic infections, Maltallia, less often during infectious anemia, Morbus maculosus, strangles and less often with contagious pleuropneumonia, infectious abortion of mares. The distinction of these encephalides is summarized in that they appear on the horizon of a determined infection, develop slowly and very often are accompanied by residual phenomena.

According to A. V. Sineva, the nervous appearances during secondary encephalides are not of one type; most often they restrict themselves to the disruption of movements as result of variations in the motor sphere

of the cortex of the brain. The clinical signs during these encephalides are characterized by a nucleic process and seldom differ from the great list of nervous signs which are observed during IEM. As a rule the secondary encephalides are accompanied by a high temperature. During histological examination there are nucleic encephalides detected in the brain of the fallen animals.

FOOD POISONING is differentiated from IEM very easily. *Artemisia taurica* is somewhat similar to IEM according to its clinical chart.

Clinical signs of poisoning develop very quickly after a horse eats grass with any type of poisonous wormwood (*Artemisia*). Icterus is absent. The course of the illness is accompanied by significant excitation; the horse tries to go forward, back, falls, stands, strikes its head against the ground. During poisoning by wormwood there are noted clonic-tonic spasms, and also jerking of the head and neck. The infection usually passes with a temperature which sometimes reaches 40 C. During dissection of the corpse there is usually some catarrhal inflammation of the gastrointestinal tract, sometimes a chart of general intoxication. During a histological of the organs there are noted significant variations in the parenchymatous organs and punctate hemorrhaging in the central nervous system.

According to clinical appearances, some poisoning of horses by sheep sorrel, horsetail, belladonna and other poisonous grasses resembles IEM. The nervous appearances during poisoning by these grasses are combined with atonia of the intestines. Excitation and oppression interchange. The mucous membranes are seldom hyperemic, dry. Single or many animals simultaneously are poisoned by these grasses.

BOTULISM is caused by a horse eating some determined food. During examination of the forage and contents of the stomach there are found toxins of botulism. Icterus of the mucous membranes is absent. The act

of swallowing is disrupted in the horses and the lower jaw hangs down. Oppression is accompanied by weakening of the animal during retention of sensitivity and a slight weakening of the reflector activity. The death rate is usually high. The course of the disease is 1-8 days. A gelatinous infiltrate in the trachea, hemorrhaging under the large intestine, epicardium, capsule of the kidneys, in the lungs and brain is detected during dissection.

The differentiation of IEM from Surru deserves attention, especially during the presence of excitation or oppression of the animal. During microscopic examination of the large drops of blood there have been found trypanosomes, and the CFA with specific antigens was positive.

When diagnosing for a disease it is necessary to consider the epizootological status of the region in which the animal is located and the locality from which the animal came.

With a differential diagnosis of IEM of horses, the epizootological conditions of its outbreak, time of year, character of the area, the degree of dissemination and degree of infection of horses and other animals are taken into consideration.

TREATMENT. Many various measures and preparations have been used against IEM of horses. There have been applications of atoxyl, rivanol, arecoline, bismuth, alcohol, albargin, mercury bi-iodide, laxative(purge), mechanical removal of the fecal masses through the rectum, catheterization, chilling of the entire body, ice on the head and others.

A hyperimmune serum has been used extensively for the treatment of IEM. According to S. N. Veshelesski, it lowers the death rate by 10-15%. Besides this, application of a hyperimmune serum was made in combination with urotropine(hexamethylenetetramine). Of 42 horses treated with hyperimmune serum with a simultaneous injection of urotropine, 27 horses survived.

The obtained data do not allow any conclusion of the high effectiveness of the serum, even during injections of high doses (200-400 ml).

Somewhat better results were obtained during the application of the hyperimmune serum in the following manner: 25-35 ml of the serum are introduced through a suboccipital puncture; after 30 minutes 200-300 ml of this same serum are subcutaneously injected into the region under the chest, or into the neck; laxative and cordial substances are introduced simultaneously with the hyperimmune serum. The treatment is repeated 3-4 times. Of 39 horses that were treated this way, 29 horses recovered.

The hyperimmune serum for medicinal purposes was prepared in the following manner. Increasing doses of virus-vaccine were introduced to horses over a period of six months (intramuscularly). At first 0.2 g of brain substance was introduced, then each successive dose was increased 0.1 g. Interval between injections-16 days. Three final doses of the virus-vaccine were introduced suboccipitally. The serums obtained by this method reliably neutralized the virus, and the CPE gave an even, positive result.

Non-specific hyperimmune serums were also tried for the treatment of ailing horses. P. P. Gerasimovich and A. I. Ulendeeva (1943) applied various serums; anti-anthrax, anti-paratyphus, anti-colibacillosis, and also serums of blood used against plague of swine. Urotropine, methylthio-bromine, camphorated oil or spirit of camphor was injected simultaneously with the serums. According to the authors, in comparative tests, the best results were obtained during the application of the swine plague serum (80% recovery). Almost identical results were obtained by these authors during utilization of the blood of convalescents. An accurate verification of the described method of treatment did not give any positive results.

A 10% solution of urotropine and a 1-2% solution of formaline have been used for the treatment of horses ailing with IEM, doses were of

100-150 ml. These measures gave inconsistent results.

From 1939 to 1949 there has been an accumulation of material on the treatment of horses with IEM by introducing 20-30 ml of a 2-3% solution of urotropine into the subarachnoid area. However, according to medicinal results, this method of injection did not differ from the intravenous injection method.

V. I. Yakushev obtained better results during suboccipital application of urotropine. According to him (1946), the suboccipital introduction of doses as much as ten times smaller than ordinary stipulated a good effect. Yakushev injected 10-20 ml of a 10% urotropine solution.

Good results were obtained in 1938-1940 during the treatment of ailing horses with urotropine and oxygen. The oxygen was introduced under the skin in doses of 10-12 liters, twice a day into the region under the chest, the urotropine, also twice daily, intravenously. It is recommended that the treatment of horses ailing with IEM be treated on the following scheme:

- 1) 10-12 liters of oxygen are introduced under the skin of the sub-thoracic region and costal region;
- 2) 300 ml of a physiological solution, in which a preliminary dilution is made of 15 grams of urotropine and 30 grams of glucose, are injected intravenously at the same time;
- 3) every 4-6 hours 20 ml of camphorated oil are introduced under the skin;
- 4) two times a day a deep enema of warm water (10-12 liters at 25-30°C), with an addition of potassium permanganate in dilutions of 1:1 000 is given;.....

Of 42 horses treated according to the scheme, 33 horses recovered and 8 fell (Shcherbatekh). According to the author, this method of treatment of horses with IEM is directed to the lowering of the acidosis, azotemia,

anoxemia, for the support of the muscular function of the heart, to the combatting of the specific agent and toxemia of the organism.

A so called 'chloridotherapy' was suggested for the treatment of horses with IEM. It is as follows. 200 ml of a hypertonic solution of sodium chloride were introduced intravenously. After 30 minutes a liter of a solution (prepared: sodium chloride 40.0, potassium chloride 1.0, sodium bicarbonate 1.0, magnesium chloride 0.5, 50% calcium chloride 5.0, distilled water 5 liters) was introduced under the skin in the region of the subthoracic or costal.

The chloridotherapy is mainly directed to the increase of the content of chloride in the blood, and the decrease of azotemia.

The veterinary commission applied the chloridotherapy method along the following scheme:

1) 150 ml of a 10% solution of sodium chloride were introduced intravenously to the ailing horses. The doses was given once daily until full recovery of the horse(3-5 days);

2) 30-60 minutes after the injection of the sodium chloride, 100 ml of a 10% solution of urotropine were injected intravenously, 30-40 g. of glucose were introduced simultaneously with the urotropine;

3) 20 ml of camphorated oil were introduced under the skin, this was repeated after 6-12 hours;

4) all the ailing horses recieved 100 g of Glauber salt with water and feed daily. The mouth area was partially sprayed with water;

5) the bladder, overfilled with urine, was massaged.

It was established that in the pathogenesis of IEM of horses the specific agent plays a determining role, it leads to a disruption of the intero-
extero-receptors by its immediate action on the nerve centers, cortex and subcortex regions of the brain. Therefore, it is very valuable lengthy

that

measures of retardation, along with the specific substances, be applied. This pathogenetic therapy can be applied by various means.

There is an accumulation of material on the treatment of horses with IEM by application of lengthy barbital or chloral-hydrate narcosis, with a simultaneous introduction of urotropine. Recovery was noted only in a few horses. Experiments on rabbits established (Shcherbatekh, Sidorenko) that the veronal retards the development of the disease only for the period of the narcosis.

An earlier isolation of the ailing horses and a timely application of medicinal measures aids in the recovery of the horses from IEM. The success of the treatment depends, besides this, on the immediate submission of the horse to rest, irregardless of where it is. Categorically it is not advisable to transport the ailing horses. The veterinary aid should be rendered on the spot, and necessary cases should have motor transportation.

Horses with IEM in open areas should be tied to a stake or other firm object. All hard objects should be removed from the areas reserved for the ailing horses. When horses are stabled, the floor should be abundantly covered with bedding, and the walls with straw mats to avert injuries to the animals. A 24 hour watch over the ailing and recovering animals should be kept by veterinary personnel.

The ailing horses are feed green grass, finely chopped root plants (carrots, beets). Water is offered without limit. Upon refusal of water it is recommended that deep enemas be made 3-4 times daily, 5-10 liters of water each.

The recovering animals are feed grass, finely chopped root plants and bran mash, and 50 g of Glauber salt per day if icterus is present⁵. The horses are gradually put to work from the 10-15th day after the clinical recovery.

SPECIFIC prophylactics. The development of a method of specific prophylactics against IEM of horses was possible only in the 30ies of this century when the etiology of this disease was clarified. A formolvaccine from the brain of spontaneously fallen horses was suggested and tried (Levenberg, Veshelesski, Shcherbatekh and others). Much time was spent on the testing of formole and carbol-glycerine vaccines, prepared from rabbit brain (Bogdanov, Yarkina, Shcherbatekh), in field tests. Ishukov and Mitovin, on the basis of data obtained during a study of the photodynamic action of methylene blue on the virus of IEM, suggested photovaccine. The latter was tried for some time in field tests with irregular results. Verifying tests, conducted by Shcherbatekh and Levashov (1947), on 6500 horses, with an equal number of control animals, established that photovaccination does not possess immunogenic properties.

A low immunizing effectiveness was established (Shcherbatekh) during testing of a weakened vaccine which had been prepared from the brain of a horse experimentally infected with the virus of IEM.

Numerous scientific-research institutes proved the adaptation of the virus of IEM of horses on chicken embryos. This served as the basis for the production of a vaccine from chicken embryos infected with the virus of IEM. M. D. Polekovski suggested a formol-embryo-vaccine, which was tried on a large number of horses. Data obtained do not allow any determined opinion of the effectiveness of this vaccine, because along with the positive indications, there are reports which state that in several regions the formolvaccine from chicken embryos does not render any immunizing action against IEM of horses.

The application (Shcherbatekh) of a 'native' vaccine prepared from a virulent brain of a rabbit gave no positive results during subcutaneous injection to horses in field and lab tests.

Effective results of immunization against IEM were obtained by Shcherbatikh and Levashov in 1943-1947. These authors proved that a suboccipital introduction of a virus-vaccine stimulates a direct and durative immunity in the inoculated horses against experimental infection. Of 76 vaccinated horses, 6 became ill after a controlled infection, 30 of 32 control horses fell. Analogical data were obtained with successive tests. The suboccipital introduction of the virus-vaccine creates a non-susceptability in the majority of the cases. The immunity appears 6-10 days after the inoculation and lasts no less than two years. This quick creation of an immunity, according to the authors, is possible because the method of injection of the vaccine allows for its immediate action on the central nervous system, as a result, there is a very quick reactive, stable reaction of the complete organism.

The suboccipital vaccination, developed in experimental conditions, has a great theoretic, as well as practical potential, because some data indicate that even in natural conditions, positive results can be obtained. The above authors vaccinated 78 horses with 43 as controls, it was established that 6 of the control horses became infected, 4 fell of this number, none of the vaccinated animals became ill.

More on the possibility of obtaining an effective immunity in practical conditions is the fact that, two horses, recovered after natural infections with encephalomyelitis, did not react to an introduction of a lethal dose of virus of IEM, while the control animals became ill and fell after the introduction of a similar dose.

With the obtainment of positive results on a large number of horses in practical conditions, the suboccipital method of vaccination could be utilized for the liquidation of the enzootic of IEM.

The complexity of the application of the suboccipital method of vaccination lead the authors to search for a more direct method of immunization.

Using the Pavlov studies, on the receptor apparatus, and the work of his students (Chernigovskii, and others), which proved the presence of proprioceptors in the muscles, as basis, Shcherbatekh and Levashov, in 1947, verified a test on the intramuscular infection of horses with positive results. This led to the development of an intramuscular vaccination against IEM. For this goal the authors selected the subrenal region, being the most abundant with specific receptors which are susceptible to the action of specific irritations-virus antigens.

Shcherbatekh and Sidorenko, in lab tests, established that the intramuscular introduction of the virus vaccine of IEM, into the lumbar region of rabbits and horses, creates a non-susceptibility in the immunized animals.

Of 34 horses vaccinated twice by this method, 29 horses didn't become ill, 5 did; of 13 control animals, 10 became ill. Almost analogous results were obtained in tests on rabbits. Of 21 twice vaccinated rabbits, infected with a lethal dose of the original virus, 19 did not become ill, while all the control animals became ill and fell. The duration of the immunity has been verified to two years. Shcherbatekh and Sidorenko developed a method of preparing and applying dry vaccine along with the application of the IEM liquid vaccine. The dry vaccine, according to the authors, has the advantage that its immunizing properties last two years in storage, that is, 7 times longer than the liquid. The results of immunization of rabbits and horses with the dry vaccine are the same as those with the liquid vaccine.

3200 horses, with an equal number of control, were vaccinated in a formerly susceptible area. For more than two years no infections were noted among the vaccinated horses.

The application of this method of vaccination, in the lumbar region, led the authors from the anatomo-physiological exclusion of this area, and from the Pavlov teachings on nervism. The organism, as a whole,

accomplishes its functional reconstruction through the nervous system. A test showed that an antigen, through the nervous system, mobilizes the organism of the animals for the protection against infection. The accepting reaction of the organism is confirmed by the positive results of complement fixing reactions (CFR) during examination of the serum of vaccinated animals.

MEASURES OF COMBATTING. In the affected areas the blood-sucking insects are considered to be the most probable vectors of the infection. Besides the specific prophylactics, there are general precautions included. These include individual protection of the animal from the bites of hematophagia and ticks, for this there are night grazings, and in the day the horses are kept in darkened buildings.

Early spring covering of water spots with oil, and a fall burning of grasses are possible measures for the extermination of the vectors.

In zones which are affected by the IEM, there are prophylactic meliorative works (drying of marshes, cleaning of brushland, etc). DDT, Hexachlorane and other preparations have been used with great success for combatting these insects. The most convenient form of applying the insecticides is by dusting or aerosols, but suspensions, emulsions and oils can be used.

A great role in the prevention of infection, including IEM of horses, is played by the measures which are directed to increasing the resistance of the organism of the animals. Proper feeding and zoohygienic conditions of stables and working areas can be possible factors in the increase of the stability of an animal to the various infectious diseases.

When it has been established that a horse is ailing from IEM, there is a quarantine and measures to exclude the possibility of dissemination. The horses in stables are divided immediately into smaller groups (15-20) and are kept separate.

The veterinary workers inform the neighboring points and areas of the appearance of IDM, organize mechanical cleaning and disinfection of the areas where the ailing and fallen horses are located.

No animals are allowed to trespass, enter or leave an infected area. The ailing, recovering, and also those horses under observation, are isolated in stables, or in special sections of open land which have been appointed for such use. Forage is not permitted out of the area until after the quarantine is lifted.

Dairy products, poultry, grain and technical cultures are allowed to leave the area only after all measures of disinfection and control have been utilized, and the regional veterinary gives a release.

In the threatened areas (neighboring brigades, etc.) the veterinary personal conduct daily inspections of each animal by means of a temperature check, apply measures for the betterment of stable, work and feed conditions, include 30-40 g of sodium chloride in the feed for each horse, conduct sessions and meetings with the horsemasters and observe the brigades for early signs of infection.

Any simple building can be used for the isolation of the horses, or they can be kept in the open. Horses suspected of becoming infected (icterus of the mucous membranes, quick fatigue, small deviations from normal) are kept in separate 'pre-isolation' areas and are subjected to prophylactic treatment with urotropine; they receive 50 g of sodium chloride each, per day.

The horses with acute courses of infection are kept in a separate group and treated. The recovering horses are also kept separate and slowly put to work after 15-20 days. The fallen animals are quickly removed-taken to a disposal plant, in the absence of one-to an animal graveyard, after being dissected. The ^{hide} ~~skin~~ of the fallen animals is

kept for 10-12 hours in a 1-2% solution of creoline, or in 'lime milk' (1:20), then it is washed with water, dried in the shade and sent for regular processing.

40 days after the last horse has been isolated, there is an accurate, inclusive, direct disinfection of the buildings and a cleaning of the area on which the ailing horses were kept, then the quarantine is lifted.

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